



**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In Re : U. S. Patent 5,610,163  
Issued : March 11, 1997  
Inventors : Banholzer, et al  
For : Esters of Thienyl Carboxylic Acids And Amino Alcohols  
And Their Quaternization Products

Mail Stop Patent Extension  
Commissioner for Patents  
P. O. Box 1450  
Alexandria, VA 22313-1450

**APPLICATION FOR EXTENSION OF PATENT TERM UNDER 35 U.S.C. § 156**

Sir:

Boehringer Ingelheim KG, a corporation of the Federal Republic of Germany (hereinafter called "the Applicant") and the owner of record of U. S. Patent No. 5,610,163 hereby applies for an extension of the term of U. S. Patent No. 5,610,163 pursuant to the provisions of 35 U.S.C. § 156 and 37 C. F. R. §§ 1.710 – 1.791.

The Applicant seeks extension of the term of U. S. Patent No. 5,610,163 for a period of 1,421 days, so that the expiration date of the patent would be changed from 11 March 2014 to 30 January 2018.

2004E-0314

APP1

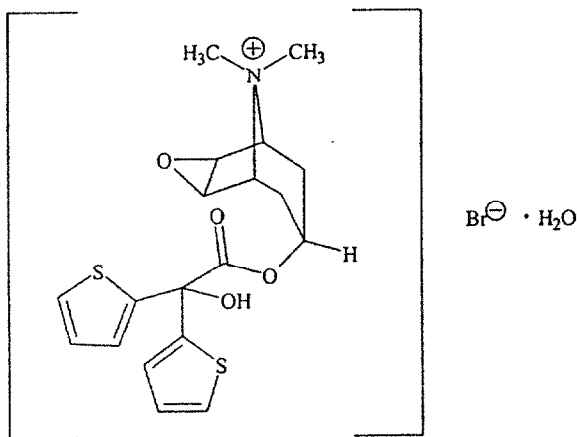
**DETAILED DESCRIPTION OF BASIS FOR THE APPLICATION**

Provided below is the information required by 37 C.F.R. § 1.740(a).

1. A complete identification of the approved product as by appropriate chemical and generic name, physical structure or characteristics

The approved product is tiotropium bromide monohydrate.

Tiotropium bromide monohydrate is the drug substance present in, and thus the active ingredient of, the new drug Spiriva® HandiHaler® (tiotropium bromide inhalation powder).<sup>1</sup> It has the following structural formula:



Tiotropium bromide is the United States Adopted Name (USAN) for the active ingredient.<sup>2</sup>

<sup>1</sup> See the text of Package Insert, which is attached hereto as Exhibit A.

<sup>2</sup> In accordance with convention, the USAN does not take into consideration the hydration state of the active ingredient.

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Ignoring the state of hydration, the active ingredient may also be identified by the following chemical names:

(1 $\alpha$ ,2 $\beta$ ,4 $\beta$ ,5 $\alpha$ ,7 $\beta$ )-7-[(hydroxydi-2-thienylacetyl)oxy]-9,9-dimethyl-3-oxa-9-azoniatricyclo[3.3.1.0<sup>2,4</sup>]nonane-bromide;

3-Oxa-9-azoniatricyclo[3.3.1.0<sup>2,4</sup>]nonane, 7-[(hydroxydi-2-thienylacetyl)oxy]-9,9-dimethyl-,bromide, (1 $\alpha$ ,2 $\beta$ ,4 $\beta$ ,5 $\alpha$ ,7 $\beta$ )-; and

6 $\beta$ ,7 $\beta$ -epoxy-3 $\beta$ -hydroxy-8-methyl-1 $\alpha$ H,5 $\alpha$ H-tropanium bromide, di-2-thienyl-glycolate.

2. A complete identification of the Federal statute including the applicable provision of law under which the regulatory review occurred

The approved product was the subject of regulatory review under the provisions of Section 505 of the Federal Food, Drug & Cosmetic Act, as amended (21 U.S.C. § 355).

3. An identification of the date on which the product received permission for commercial marketing or use under the provision of law under which the applicable regulatory review period occurred

The product received permission for commercial marketing or use under the provisions of Section 505 of the Federal Food, Drug & Cosmetic Act (21 U.S. C. § 355) on 30 January 2004, the date New Drug Application (NDA) No. 21-395 was approved by the United States Food and Drug Administration.

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4. An identification of each active ingredient in the drug product and as to each active ingredient, a statement that it has not been previously approved for commercial marketing or use under the Federal Food, Drug & Cosmetic Act, the Public Health Service Act, or the Virus-Serum Toxin Act

The sole active ingredient in the new drug product Spiriva® HandiHaler® (tiotropium bromide inhalation powder) is tiotropium bromide monohydrate.

The active moiety or component of the active ingredient is tiotropium. Tiotropium is the positively charged moiety in the structural formula for tiotropium bromide provided above.

It is the Applicant's information and belief that neither tiotropium bromide (regardless of hydration state) nor tiotropium (regardless of hydration state or counter-anion) have previously been approved for commercial marketing or use under the Federal Food, Drug & Cosmetic Act, the Public Health Service Act, or the Virus-Serum-Toxin Act.

5. A statement that the application is being submitted within the sixty day period permitted for submission pursuant to § 1.720(f) and an identification of the date of the last day on which the application could be submitted

This application is being submitted within the sixty day period permitted for submission pursuant to § 1.720(f). Such sixty day period will expire on 30 March 2004.

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6. An identification of the patent for which an extension is being sought by the name of the inventor, the patent number, the date of issue, and the date of expiration

The patent for which an extension is being sought is U. S. Patent No. 5,610,163. It issued on 11 March 1997. Absent any extension which may be granted as a result of the present application, it will expire on 11 March 2014.<sup>3</sup> The inventors named in the patent are Rolf Banholzer, of Ingelheim am Rhein, Rudolf Bauer, of Wiesbaden, and Richard Reichel, of Ingelheim am Rhein, all of the Federal Republic of Germany.

7. A copy of the patent for which extension is being sought, including the entire specification (including claims) and drawings

A copy of U. S. Patent No. 5,610,163, the patent for which extension is being sought, including the entire specification (including claims) and drawings is attached hereto as Exhibit B.

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<sup>3</sup> The term of U. S. Patent No. 5,610,163 was determined in the following manner: It issued on 11 March 1997 and results from an application (Ser. No. 405,111) filed on 16 March 1995. Thus, its term is to be determined in accordance with 35 U.S.C. §154(c)(1), which states, "The term of a patent that is in force on or that results from an application filed before the date that is 6 months after the date of the enactment of the Uruguay Round Agreements Act shall be the greater of the 20-year term as provided in subsection (a), or 17 years from grant, subject to any terminal disclaimers." (The Uruguay Round Agreements Act was enacted on 8 December 1994.) Further, U. S. Patent No. 5,610,163 contains a specific reference to several earlier filed applications under 35 USC §120, the earliest of which is Ser. No. 838,724, filed 13 March 1992. Thus, its term is the greater of 20 years from the earliest filed application under 35 USC 120 (13 March 1992) as provided by 35 U.S.C. § 154(a), or 17 years from grant (11 March 1997). The term calculated as 17 years from grant yields the greater result. Accordingly, the patent will expire on 11 March 2014.

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8. A copy of any disclaimer, certificate of correction, receipt of maintenance fee payment, or reexamination certificate issued in the patent

Copies of the three (3) Certificates of Correction issued for U. S. Patent No. 5,610,163 are attached hereto as Exhibit C.

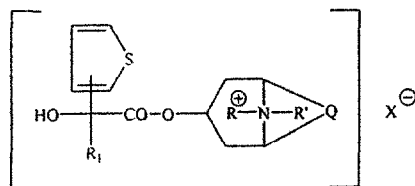
Copies of the maintenance fee statement showing the status of payment of the first maintenance fee as PAID is attached hereto as Exhibit D.

9. A statement that the patent claims the approved product or a method of using or manufacturing the approved product, and a showing which lists each applicable patent claim and demonstrates the manner in which each applicable patent claim reads on the approved product or method of using or manufacturing the approved product

U. S. Patent No. 5,610,163 claims the approved product.

The applicable patent claims which read on the approved product are Claims 1 – 5, 7, 11 and 14. The text of these claims, as amended by the Certificates of Correction dated 4 July 2000 and 3 December 2002, is provided by Exhibit E.

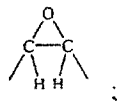
Claim 1 reads on the approved product because the approved product, tiotropium bromide (regardless of its state of hydration), is a compound of the formula



wherein

Q is a group of the formula

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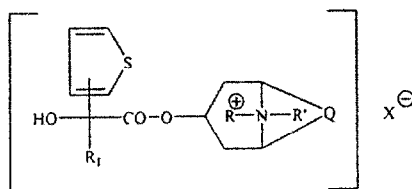


R and R' are each methyl (which is a C<sub>1</sub>-C<sub>4</sub>-alkyl);

R<sub>1</sub> is thienyl; and,

X<sup>-</sup> is a bromide ion<sup>-</sup> (which is a physiologically acceptable anion).

Claims 2, 3 and 4 read on the approved product because tiotropium bromide (regardless of its state of hydration) is a compound of the formula



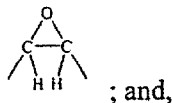
wherein

R is CH<sub>3</sub>;

R' is CH<sub>3</sub>;

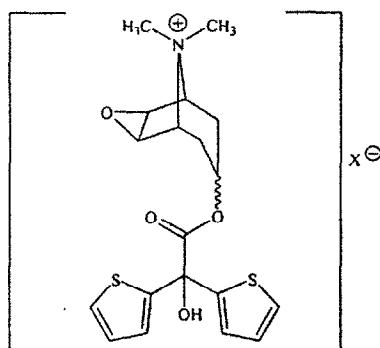
R<sub>1</sub> is thienyl;

Q is a group of the formula



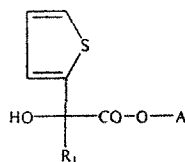
X<sup>-</sup> is a bromide ion (which is a physiologically acceptable anion).

Claim 5 reads on the approved product because tiotropium bromide (regardless of its state of hydration) is a compound of the formula



wherein X- is a bromide ion (which is a physiologically acceptable anion).

Claim 7 reads on the approved product because tiotropium bromide (regardless of its state of hydration) is a compound of the formula



wherein R<sub>1</sub> is 2-thienyl and A is 3α-(6β, 7β-epoxy)-tropanyl methobromide.

Claim 11 reads on a method of using the approved product because it is directed to a method for treating chronic obstructive bronchitis which comprises administering, by inhalation, to a subject suffering from the same, a therapeutic amount of a compound in accordance with claims 1, 2, 3, 4 or 7. It has already been established above that claims 1, 2, 3, 4 and 7 read on the approved product, tiotropium bromide (regardless of hydration state). Further, the approved indication for the new drug Spiriva® HandiHaler® (tiotropium bromide inhalation powder) is "the long-term, once daily, maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD) including chronic bronchitis and emphysema." The use recited in claim 11 may fairly be said to correspond to the approved indication for the new drug, of which tiotropium bromide is the sole active ingredient.

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Claim 14 reads on the approved product because it is directed to a pharmaceutical composition, for administration by inhalation, suitable for the treatment of chronic obstructive bronchitis or slight to moderately severe asthma, which comprises a compound in accordance with claims 1, 2, 3, 4, or 7. It has already been established that the sole active ingredient of the approved new drug is a compound in accordance with claims 1, 2, 3, 4 and 7. The new drug is administered by inhalation and is, as established above, suitable for the treatment of COPD, including chronic bronchitis.

10. A statement beginning on a new page, of the relevant dates and information pursuant to 35 U.S.C. 156(g) in order to enable the Secretary of Health and Human Services or the Secretary of Agriculture, as appropriate, to determine the applicable regulatory review period as follows:

*(Only subparagraph (i) is applicable. Subparagraph (i) reads as set forth below.)*

(i) For a patent claiming a human drug, antibiotic, or human biological product:

(A) The effective date of the investigational new drug (IND) application and the IND number;

(B) The date on which a new drug application (NDA) or a Product License Application (PLA) was initially submitted and the NDA or PLA number; and

(C) The date on which the NDA was approved or the Product License issued.

The required statement appears in Exhibit F.

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11. A brief description beginning on a new page of the significant activities undertaken by the marketing applicant during the applicable regulatory review period with respect to the approved product and the significant dates applicable to such activities

The required brief description appears in Exhibit G.

12. A statement beginning on a new page that in the opinion of the applicant the patent is eligible for the extension and a statement as to the length of the extension claimed, including how the length of extension was determined

The required statement appears in Exhibit H.

13. A statement that the applicant acknowledges a duty to disclose to the Director of the United States Patent and Trademark Office and the Secretary of Health and Human Services or the Secretary of Agriculture any information which is material to the determination of entitlement to the extension sought

The undersigned attorney for Applicant acknowledges, on behalf of the Applicant, a duty to disclose to the Director of the United States Patent and Trademark Office and the Secretary of Health and Human Services any information that is material to the determination of entitlement to the extension sought.

14. The prescribed fee for receiving and acting upon the application for extension

The prescribed fee of \$1,120 pursuant to 37 C.F.R. § 1.20(j) may be charged to Deposit Account No. 02-2955. In addition, the Commissioner is hereby authorized to charge any additional fees necessary, or to refund any overpayment, to Deposit Account 02-2955. A duplicate copy of this Fee Authorization paper is also submitted herewith.

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15. The name, address and telephone number of the person to whom inquiries and correspondence relating to the application for patent term extension are to be directed

Direct all correspondence relating to this application to:

Michael P. Morris  
Boehringer Ingelheim Corporation  
900 Ridgebury Road, P. O. Box 368  
Ridgefield, CT 06877-0368

Phone No. (203) 798-5285  
Fax No. (203) 798-4408  
E-mail: mmorris2@rdg.boehringer-ingelheim.com

This application is accompanied by two additional copies of such application (for a total of three copies).

Pursuant to 37 C.F.R. § 1.730(b)(2), this application is signed by a registered practitioner on behalf of the patent owner. Proof that this practitioner is authorized to act on behalf of the patent owner is supplied by the APPOINTMENT OF ATTORNEY FOR PURPOSES OF PATENT TERM EXTENSION UNDER 35 U.S.C. §156 that is attached hereto as Exhibit I.

**BOEHRINGER INGELHEIM KG**

Date: March 15, 2004

By: Michael P. Morris  
Michael P. Morris  
Attorney for Applicant  
Registration No. 34,513